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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/736,051	12/13/2000	Hua Zhu Ke	PC9344BRTR	6748

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EXAMINER	
LEARY, LOUISE N	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 10/08/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/736,051	KE ET AL.	
	Examiner	Art Unit	
	Louise N. Leary	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-30,33-42,45-50,52-55,57-62,65-69,72-75,79,80,84-89,92-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-4,6-14,16-30,33-42,45-50,52-55,57-62,65-69,72-75,79,80,84-89 and 92* is/are allowed.

6)☒ Claim(s) *93,95,97,99,101,102,104 and 106* is/are rejected.

7)☒ Claim(s) *94,96,98,100,103,105,107 and 108* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

1. The FINALITY of the office action dated February 4, 2003 has been withdrawn in favor of the office action on the merits below.

2. Claims 1-4,6-14,16-30,33-42,45-50,52-55,57-62,65-69,72-75,79-80,84-89,92, and 93-108 are pending in this application.

Claims 5, 15, 31-32, 43-44, 51, 56, 63-64, 70-71, 76-78, 81-83, and 90-91 have been canceled per applicant's request.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 93, 97, 101-102, and 106 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lax et al (Endocrinology, V. 113(5), p 1043-1055,(1983).

Lax et al disclose administration of combinations comprising an estrogen antagonist/agonist compound and human growth hormone (hGH). Lax et al disclose

administering and evaluating physiological activity of female rat castrates administered hGH and tamoxifene. See page 1045, column 1. In addition, Lax et al describe simultaneously administering tamoxifen and growth hormone (GH) and evaluating target tissues in female castrates. Note the entire reference. Thus, Lax et al disclose the combination claimed except for using the word "secretagogue".

However, regarding the use of the word "secretagogue", Lax et al disclose combining an estrogen antagonist/agonist compound and human growth hormone (hGH), administering the compounds to female rat castrates for evaluation of physiological activity. Hence, it is noted that Lax et al disclose all the claim limitations except for the inherent secretagogue function of the hGH in the pharmaceutical combination which anticipates or renders obvious the claimed invention.

Therefore, the burden of proof is on applicants to show patentably distinct differences between the Lax et al disclosure and the present invention as claimed.

4. Claims 93, 95, 97, 99, 101-102, 104 and 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gertz et al (WO 95/11029, April 1995) in combination with Wronski et al (Endocrinology, V.132(2), pp.823-831,(1993) and Evans et al (Endocrinology, V. 134(5), p 2283-2288, (1994) Abstract Only.

Gertz et al disclose a combination comprising a bisphosphonate compound and a growth hormone secretagogue. Gertz et al disclose the combinations have been used to treat osteoporosis in elderly patients. In addition, Gertz et al disclose pharmaceutical compositions comprising the combination with an acceptable pharmaceutical carrier.

Note this entire document. Further, Gertz et al disclose "bisphosphonates (bisphosphonic acids) are known to inhibit bone resorption and are useful for the treatment of bone lithiasis..." See page 1, lines 5-6. Thus, Gertz et al disclose the instant combination as well as the method of making and/or using the combinations claimed except for addressing the use of an estrogen agonist/antagonist compound and raloxifene as an estrogen agonist/antagonist.

However, regarding the use of an estrogen agonist/antagonist compound in combinations for treating osteoporosis as claimed in the instant invention, Wronski et al disclose "[Estrogen (1,2) and bisphosphonates (3-5) have been shown to depress bone resorption and increase bone density modestly in women with established osteoporosis, but their ability to completely restore the lost bone is uncertain."] See page 823, column 1. Also, Wronski et al show results from a comparative study of estrogens and bisphophonates for treating lost bone mass in ovariectomized rats. See this entire reference. As a result, Wronski et al provided sufficient guidance for skilled artisans to use estrogens and bisphophonates interchangeably in pharmaceutical combinations for treatment of bone mass loss prior to the time this invention was made.

With respect to the use of raloxifene in the instant invention, Evans et al disclose raloxifene is an estrogen agonist/antagonist having potent estrogenic activity on bone resorption and may be useful in protecting against osteoporosis. Note the entire abstract. Thus, Evans et al address the selected use of raloxifene as an estrogen agonist/antagonist in pharmaceutical combinations for treating osteoporosis.

Hence, Gertz et al disclose the invention claimed except for describing the relationship between bisphosphonate and estrogen agonist/antagonist compounds in combinations with GH secretagogue and the selection of raloxifene as an estrogen agonist/antagonist compound for treating osteoporosis which was respectively provided by Wronski et al reporting that bisphosphonates have been used interchangeably with estrogen compounds in pharmaceuticals to treat osteoporosis and Evans et al disclosure that raloxifene is an estrogen agonist/antagonist having potent estrogenic activity on bone resorption and may be useful in protecting against osteoporosis before this invention was made.

It would have been obvious to one having ordinary skill in this art at the time this invention was made to provide a combination comprising an estrogen agonist/antagonist and a growth secretagogue for use in a method for treating osteoporosis because Gertz et al disclose combinations comprising growth hormone secretagogue and bisphosphonate for use in a method that treats osteoporosis except for addressing guidance for substituting an estrogen agonist/antagonist for a bisphosphonate that was provided earlier by Wronski et al showing the bisphosphonate was interchangeable with an estrogen agonist/antagonist in pharmaceuticals for treating osteoporosis and except for stating the raloxifene is an estrogen agonist/antagonist which renders the present invention obvious.

5. Claims 94, 96, 98,100, 103, 105 and 107-108 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. The Patchett et al reference (Proc. Natl. Acad. Sci. USA, Fol. 92, pp 7001-7005, July 1995) disclose administering nifedipine about 30 or 60 sec before addition of a potent, growth hormone (GH) secretagogue (designated as L-163,191 and as the mesylate salt, MK-0677) and has been cited to further show the state o this art.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise N. Leary whose telephone number is (703) 308-3533. The examiner can normally be reached on Monday to Friday from 10 am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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LOUISE N. LEARY
PRIMARY EXAMINER

September 27, 2003